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Original Article

Advanced sleep–wake rhythm in adults born prematurely: confirmation by actigraphy-based assessment in the Helsinki Study of Very Low Birth Weight Adults

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ABSTRACT

Objective: Previous studies have suggested a propensity towards morningness in teenagers and adults born preterm. We set out to study sleep in a subsample from The Helsinki Study of Very Low Birth Weight Adults cohort, with emphasis on sleep timing, duration, and quality. We compared young adults who were born prematurely at very low birth weight (VLBW; <1500 g) with controls born at term.
Methods: We measured sleep by actigraphy in young adults aged 21–29 years. A total of 75 individuals (40 VLBW and 35 controls) provided adequate data. Group differences in sleep parameters were analyzed using *t*-test and linear regression models.
Results: VLBW adults woke up on average 40 min earlier [95% confidence interval (CI), 9–70] and reported 40 min earlier get up time (95% CI, 8–71) than did the controls. The difference remained after adjustment for confounders. We found no group difference in sleep duration or measures of sleep quality.
Conclusion: Our findings of earlier rising in the VLBW group are suggestive of an advanced sleep phase in that group. These results reinforce previous suggestions that chronotype may be programmed early during life.

1. Introduction

About 0.8–1.5% of children born in developed countries today are born prematurely (<37 completed weeks of gestation) with very low birth weight (VLBW; <1500 g) [1,2]. In earlier decades, being born preterm with VLBW implied a low chance of survival. For example, in the 1960s, only about half of live-born VLBW infants in industrialized countries survived, whereas 85–90% do so today [1,3,4]. This is mainly due to the remarkable advances witnessed in modern neonatal intensive care from the 1970s onwards, such as improvements in ventilation strategies and introduction of antenatal glucocorticoids and surfactant. Therefore there is today a considerable number of young adults who were born with VLBW and whose health prospects may differ from those of individuals born at term.

Previous studies indicate that some mental health problems such as symptoms of depression and attention deficit/hyperactivity disorder (ADHD) are more common among people born preterm or subgroups of them [5–8]. Differences regarding somatic health have also been described, eg higher levels of insulin resistance [9] and blood pressure [9–11].

Abnormalities in sleep are linked to many of the aforementioned conditions associated with prematurity, including ADHD, insulin resistance, hypertension, and depression [12–15]. The question arises whether sleep characteristics of ex-preterms differ from those of term-borns. If they do differ, this could be a link between preterm birth and prematurity-associated health sequelae. Whereas sleep of ex-preterms during early childhood has been studied to some extent, yielding somewhat discrepant results [16–19], only a few

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studies range beyond early childhood [20], not to mention adulthood [21].

In our previous study performed in 2004–2005 [21] using actigraphy and questionnaires, it was found that VLBW adults went to bed earlier than their term-born control group. That was a post-hoc finding and we set out to confirm this in a prospective setting. We subsequently reported that adults born with VLBW have a propensity towards morningness, a trait indicating personal preference for an early rhythm [22]. The current follow-up study aimed to further validate our earlier findings in a somewhat different subsample, and with improvements in methodology. We used actigraphy to assess sleep timing, sleep duration, and sleep quality. We hypothesized that VLBW adults, as compared with term-born controls, would show signs of an earlier sleep phase.

2. Methods

2.1. Participants

The Helsinki Study of Very Low Birth Weight Adults is a case–control cohort study that has been described in detail previously [9]. The original cohort consisted of 335 VLBW children treated in the neonatal intensive care unit (NICU) of the Children's Hospital at Helsinki University Central Hospital between January 1978 and December 1985. In 2003, we traced the original VLBW cohort using the National Population Register, and invited to a clinical study those 255 individuals (76%) who were still living in the greater Helsinki area. A comparison group of 314 individuals was formed, consisting of the next singleton, term-born (gestational age ≥37 weeks), same-sex, non-SGA child born in the same hospital after each corresponding VLBW birth.

All these individuals (255 VLBW and 314 term-born controls) were invited to participate in a first clinical study, consisting of extensive cardiovascular and metabolic assessments and detailed questionnaires regarding medical history, mental health, socio-economic characteristics, and physical activity. This examination was performed in the years 2004–2005 and was completed by 338 individuals (166 VLBW, 65% of those invited; and 172 term controls, 55% of those invited).

Several results from this first clinical study have been published, eg data on blood pressure [9,23], glucose regulation and insulin resistance [9], symptoms of depression [7] and attention deficit/hyperactivity disorder [8], cognitive functions [24,25], and personality [26]. In addition, data on sleep quality and sleep duration, by means of actigraphy and questionnaire, have been reported [21,27].

During 2007–2008, a follow-up study was performed. Of the previous 338 participants, 11 lived abroad, four refused to be contacted again, one person was developmentally delayed, two could not be traced, and seven did not fulfil the inclusion criteria for an intravenous glucose tolerance test that was performed in conjunction with the follow-up, leaving 313 persons who were eligible and invited. Of these 313 persons, 218 (69.6%) participated (113 VLBW, 105 controls).

In conjunction with this follow-up examination, an actigraphy-based sleep study was again conducted within a subsample. All 218 participants were offered an actigraph if there was one available at the time, resulting in 116 individuals who were asked to take part in the actigraphy study. Of these 116 individuals, 106 produced 1 or more nights of actigraphy data (57 VLBW, 49 controls). A total of 48 participants (33 VLBW and 15 controls) participated in both the original actigraphy study 2004–2005 and the follow-up actigraphy study 2007–2008.

There were no statistically significant differences in the perinatal and young adult characteristics presented in Table 1 between the participants in the actigraphy study and those who participated in the rest of the second clinical examination, except regarding employment; the actigraphy participants were more likely to be in paid employment ($P = 0.011$) both in the VLBW group and the control group. Each participant gave written informed consent to this study, which was approved by the local ethics committee and was carried out according to the Declaration of Helsinki.

Table 1
Characteristics of the VLBW and control groups.

Variable	VLBW ($n = 40$) Mean (SD)	Control group ($n = 35$) Mean (SD)	*P*-value
Birthweight (g)	1096 (224)	3640 (514)	<0.001[a]
Gestational age (weeks)	29.2 (2.5)	40.0 (1.2)	<0.001[a]
Relative birthweight SD[b]	−1.4 (1.6)	0.23 (1.1)	<0.001[a]
Singleton pregnancy, *n* (%)	35 (87.5)	35 (100)	0.030[c]
SGA[b], *n* (%)	15 (37.5)	0 (0.0)	<0.001[c]
Maternal pre-eclampsia, *n* (%)	7 (17.5)	2 (5.7)	0.12[c]
Maternal smoking during pregnancy, *n* (%)	7 (18.9)	6 (17.1)	0.85[c]
Firstborn, *n* (%)	16 (41.0)	15 (42.9)	0.87[c]
Caesarean, *n* (%)	22 (56.4)	4 (11.4)	<0.001[c]
Daily smoking, *n* (%)	6 (15.0)	8 (22.9)	0.38[c]
Using antidepressants, *n* (%)	6 (15.0)	1 (2.9)	0.071[c]
Paid employment, *n* (%)	25 (62.5)	16 (45.7)	0.15[c]
Men, *n* (%)	15 (37.5)	7 (20.0)	0.097[c]
Age during study (years)	25.0 (2.1)	24.9 (2.2)	0.81[a]
Body mass index (kg/m^2)	23.1 (4.1)	24.1 (5.3)	0.35[a]
Parental education			0.18[c]
Elementary school, *n* (%)	5 (12.5)	2 (5.7)	
High school level, *n* (%)	14 (35.0)	6 (17.1)	
Intermediate level, *n* (%)	7 (17.5)	10 (28.6)	
University degree, *n* (%)	14 (35.0)	17 (48.6)	

VLBW, very low birthweight; SD, standard deviation; SGA, small for gestational age. Missing data for the following variables: maternal smoking during pregnancy ($n = 3$), firstborn ($n = 1$), caesarean ($n = 1$).
[a] *t*-Test.
[b] Relative birthweight is given in SD units, e.g. SGA (small for gestational age) = birthweight below −2 SD of the Finnish mean after adjusting for sex and gestational age.
[c] χ^2-Test.

2.2. Actigraphy

For sleep measurement we used actigraphy (Actiwatch AW4 model, Cambridge Neurotechnology Ltd, Papworth Everard, UK). An actigraph is an accelerometer that looks like a wristwatch and is usually worn on the non-dominant wrist. The actigraph recognizes movement with piezoelectric beams and stores the information digitally. When connected to a computer thereafter, the recorded movement data can be analyzed. In this study the data were analyzed with the algorithm incorporated in the Actiwatch Activity & Sleep Analysis V 5.42 software [28], to determine whether the participant was asleep or awake during a certain epoch. High frequency of movement within an epoch is indicative of wakefulness, that is, if the activity count exceeds a predefined threshold value the epoch is scored as wake. If the activity level does not surpass the threshold during several consecutive epochs, the wearer is considered to be asleep. The threshold sensitivity can be further regulated within the program's sensitivity setting. The validity of actigraphy, as compared with the "gold standard" in sleep research – polysomnography – has been shown to be good in several studies, producing epoch-by-epoch sleep–wake agreement rates of >90% [29–32]. Despite the possible limitations of actigraphy when it comes to detection of sleep start [33], actigraphy is good at detecting activity changes, which suffices to be of interest when studying circadian phase changes.

The participants kept a sleep diary in which they reported when the actigraph was not worn (when showering, etc.) and when they

closed (bedtime) and opened (wake-up time) their eyes when going to sleep or getting up. The use of sleep diaries is considered an important supplement for increasing the validity of actigraphy [34]. The participants were also asked to press a button (event marker) in the actigraph at these specific times.

2.3. Actigraphy data analysis

The participants were instructed to wear the actigraph for a minimum of 5 consecutive days, only to remove it when showering, washing dishes, etc., and to carefully register these activities both by means of the diary and by pressing the "event marker" button. One-minute epochs and medium sensitivity were chosen, as recommended by the manufacturer.

The following parameters with their definitions were used – bed time: inserted time when lights are switched off/eyes are closed (this is set by the analysis software reading an event marker); get-up time: inserted time when lights are switched on/eyes are opened (this is set by the analysis software by reading an event marker); sleep start: the start of sleep as determined automatically by the sleep algorithm; sleep end: the end of sleep as determined automatically by the sleep algorithm; actual sleep time: the amount of sleep as determined by the algorithm; sleep efficiency: actual sleep time/ time in bed; sleep latency: the latency before sleep onset following bedtime; fragmentation index: the addition of percentage minutes moving; time in bed: the difference between the get-up and bed times; and wake after sleep onset (WASO): time in bed minus sleep latency minus actual sleep time.

The data were analyzed by visually comparing the graphically displayed activity data with the sleep diaries and event markers to determine potential discrepancies. Individual nights were excluded from the analysis for one or more of the following reasons: if the actigraph was not in use during the night; if information on bedtime was missing (both sleep diary and event marker); if all information on wake-up time was missing and the activity pattern of the actigraphy data was not unequivocally interpretable; if the sleep log information was missing and the event markers were not unequivocally interpretable; if both sleep log information and event markers were missing although the actigraph had been in use; or if the registered activity data did not correspond with the sleep log or the event markers.

The 106 participants with 1 or more nights of actigraphy data produced a total of 482 recorded nights, of which 51 nights (10.6%) were excluded. All participants with less than three analyzed and accepted nights were excluded (11 with 2 nights, three with 1 night, and 10 with 0 nights, yielding a total of 24 [20.7%] excluded participants from the original 116). One participant with cerebral palsy was excluded as neurosensory impairment is likely to interfere with sleep and 16 participants were excluded because they reported having night shifts at work. Thus 75 participants (40 VLBW and 35 from the control group) with a total of 331 nights (individual mean, 4; range, 3–7) were used in the analysis of the data. The data were averaged for each participant over the nights with recordings and the mean values were used in the analyses. Weekend nights (Friday–Saturday, Saturday–Sunday) and weekday nights were also analyzed separately.

2.4. Statistical analysis

Group differences were analyzed with *t*-test and χ^2-test. Sleep latency was transformed logarithmically before analysis to improve normality. The group differences in sleep variables are shown in Table 2.

Multiple linear regression models were computed to test group differences in sleep outcomes while controlling for confounding factors, such as age, sex, parental education (the highest educational attainment achieved by either parent, dummy-coded with the least educated group as reference), state of employment (paid employment yes/no), use of tobacco, and use of antidepressants. Three regression models are presented in Table 3: model 1 (unadjusted), model 2 (adjusted for sex and age), and model 3 (full model with all variables).

The tests were two-sided and the α-level was set at 0.05. The statistical analyses were performed by PASW Statistics 17.0 (Hong Kong).

To investigate whether group differences were dependent on sex the interaction term 'sex X study group' was analyzed for all sleep variables, setting the interaction term α-level at 0.01 to avoid false positives. All interaction terms were non-significant and hence the results are reported for men and women together.

3. Results

Table 1 shows the clinical characteristics and background variables of the participants. By design, the VLBW group had lower mean birth weight and shorter gestational age and they were more likely to be smaller for gestational age. The VLBW group and the control group had similar sex and age distributions. No significant differences existed regarding paid employment.

Table 2 shows comparisons of sleep variables between the VLBW and the term-born groups. There were no differences in fragmentation index, bedtime, sleep start, actual sleep time, sleep efficiency, wake after sleep onset, and sleep latency. Whereas the VLBW subjects and term-born participants had similar bedtime and sleep start times, VLBW subjects got up earlier in the morning. This was indicated by the times that the participant recorded awakening by pressing the event marker (40 min 1 s earlier get-up time; $P = 0.012$) and by the times that the actigraphy software calculated as the time of awakening (40 min 13 s earlier sleep end; $P = 0.011$).

Next, we explored the distribution of weekend and weekday nights in the sample. There was no difference in the amount of registered weekend nights between the VLBW and term-born groups (38 and 44, $P = 0.36$). In separate analyses of weekend nights, the VLBW group (as compared with controls) got up even earlier than in combined analyses, get-up time difference 1 h 3 min ($P = 0.011$) and sleep end 1 h 4 min ($P = 0.009$). No significant group difference was seen in analyses of weekday nights.

Adjustments for confounders (ie, sex, age, parental education, state of employment, use of antidepressants, and current smoking), did not change the results, as shown in Table 3. We also examined the effect of the seasonal distribution of the sampling (actigraphy registration month dummy-coded into four photoperiods: May to July, August to October, November to January, and February to April), and found that our results remained regardless of photoperiod.

4. Discussion

We found in an objective assessment by actigraphy that VLBW young adults got up ~40 min earlier in the morning than did their peers born at term. This finding was even more pronounced on weekend mornings, when waking up is less likely to be regulated by external demands such as start of work or study. This result reinforces previous suggestions that VLBW adults have an advanced sleep phase. No significant group differences were seen in measures of sleep quality (sleep latency, sleep efficiency, sleep fragmentation, wake after sleep onset) or duration (actual sleep time).

This study is consistent with the study performed by Strang-Karlsson et al. [21]. in a different subsample (89 VLBW and 78 term-born controls) of the same cohort during 2004–2005. To our knowledge theirs is the only other study that has used actigraphy in adults born with VLBW. That study showed, as a post-hoc finding,

Table 2
Comparison of sleep variables across groups.

	Units	Control group Mean (SD)	VLBW Mean (SD)	Mean difference, control–vs VLBW group (95% CI)	*P*-value
Sleep variables, both weekend and weekday nights (35 controls, 40 VLBW)					
Sleep end	h:min:s	08:25 (01:03)	07:45 (01:09)	−0:40:13 (−1:10:47 to −09:39)	0.011
Get-up time	h:min:s	08:27 (01:04)	07:47 (01:10)	−0:40:01 (−1:11:04 to −08:58)	0.012
Sleep start	h:min:s	00:25 (01:06)	00:06 (01:19)	−0:18:52 (−52:31 to 14:48)	0.27
Bedtime	h:min:s	00:10 (01:04)	23:55 (01:15)	−0:16:13 (−48:03 to 16:34)	0.34
Actual sleep time	h:min:s	07:00 (00:47)	06:46 (00:58)	−0:14:30 (−38:50 to 09:50)	0.24
Sleep latency	min:s	13:51 (13:54)	10:41 (10:21)	−2:48 (−8:45 to 2:25)	0.20[a]
Sleep efficiency	%	84.6 (7.0)	85.6 (6.9)	0.97 (−2.2 to 4.2)	0.55
Wake after sleep onset	h:min:s	1:00:24 (0:28:44)	0:54:41 (0:25:07)	−0:05:43 (−0:18:07 to 0:06:41)	0.36
Fragmentation index		28.1 (10.0)	27.5 (10.2)	−0.63 (−5.3 to 4.0)	0.79
Sleep variables, only weekend nights (26 controls, 21 VLBW)					
Sleep end	h:min:s	9:53:36 (1:15:34)	8:49:43 (1:24:00)	−1:03:53 (−1:50:49 to −0:16:57)	0.009
Get-up time	h:min:s	9:57:09 (1:18:22)	8:54:39 (1:22:07)	−1:02:31 (−1:49:49 to −0:15:12)	0.011
Sleep start	h:min:s	25:04:52 (1:36:34)	24:17:07 (1:21:04)	−0:47:45 (−1:40:56 to 0:05:26)	0.077
Bed time	h:min:s	24:56:16 (1:36:24)	24:09:09 (1:22:42)	−0:47:08 (−1:40:39 to 0:06:24)	0.083
Actual sleep time	h:min:s	7:43:16 (1:16:23)	7:35:49 (1:29:31)	−0:07:28 (−0:56:12 to 0:41:17)	0.76
Sleep latency	min:s	8:36 (7:51)	7:59 (7:32)	−0:37 (−5:11 to 3:56)	0.73[a]
Sleep efficiency	%	85.89 (7.26)	86.73 (5.80)	0.84 (−3.09 to 4.77)	0.67
Wake after sleep onset	h:min:s	1:09:01 (0:40:04)	1:01:43 (0:27:20)	−0:07:18 (−0:27:59 to 0:13:22)	0.48
Fragmentation index		28.18 (11.15)	28.20 (11.13)	0.022 (−6.56 to 6.61)	0.995
Sleep variables, only weekday nights (35 controls, 40 VLWB)					
Sleep end	h:min:s	7:49:09 (1:10:35)	7:26:08 (1:24:45)	−0:18:10 (−0:59:12 to 0:13:12)	0.21
Get-up time	h:min:s	7:50:38 (1:11:00)	7:27:53 (1:25:05)	−0:22:45 (−0:59:07 to 0:13:37)	0.22
Sleep start	h:min:s	24:06:59 (1:07:39)	23:58:41 (1:24:17)	−0:08:18 (−0:43:49 to 0:27:13)	0.64
Bedtime	h:min:s	23:51:47 (1:06:18)	23:47:06 (1:18:35)	−0:04:42 (−0:38:25 to 0:29:02)	0.78
Actual sleep time	h:min:s	6:46:03 (0:45:47)	6:36:04 (0:58:06)	−9:59 (−34:18 to 14:20)	0.42
Sleep latency	min:s	14:56 (15:07)	11:35 (11:46)	−3:06 (−9:33 to 2:51)	0.18[a]
Sleep efficiency	%	84.86 (7.02)	85.57 (7.11)	0.71 (−2.55 to 3.97)	0.67
Wake after sleep onset	h:min:s	0:57:36 (0:28:26)	0:53:08 (0:25:05)	−0:04:28 (−0:16:47 to 0:07:50)	0.47
Fragmentation index		28.09 (10.60)	27.87 (10.76)	−0.22 (−5.15 to 4.71)	0.93

VLBW, very low birthweight; SD, standard deviation; CI, confidence interval.
A negative value indicates an earlier time or shorter duration in the VLBW group.
[a] Because sleep latency had a right-skewed distribution, the *P*-value was calculated with Mann–Whitney *U*-test.

that the VLBW group went to bed earlier. Together with our present finding of earlier sleep end, these studies together and independently suggest an association between VLBW and an advanced sleep phase.

The findings are also in line with an actigraphy study performed on 12-month-old infants showing that VLBW infants had significantly earlier sleep onset and offset times than their term-born controls [16]. In the same study the nocturnal sleep duration among the VLBW infants was shorter, whereas there was no such difference in adults. Gössel-Symank et al. [17]. also used actigraphy in analyzing the sleep of premature children at age 20 months. In that study, a trend towards shorter night-time sleep was shown, and sleep was less restful. A recent study on adolescents aged 16–19 years by Hibbs et al. [20]. also shows earlier bed and wake times among the prematurely born (<37 weeks gestational age and admitted to the NICU for at least one week).

In addition to these objectively measured behavioural findings, chronotype can be assessed by measuring an individual's preferences on a "morningness–eveningness" scale. In a partly different subsample from the same cohort, Strang-Karlsson et al. [22]. used the Morningness–Eveningness Questionnaire (MEQ) and found that the VLBW group had a propensity for morningness. The study cor-

Table 3
Group comparisons of sleep variables using linear regression models.

Sleep variables	Unit	Model 1 Mean difference, control vs VLBW group (95% CI)	Model 1 *P*-values	Model 2 Mean difference, control vs VLBW group (95% CI)	Model 2 *P*-values	Model 3 Mean difference, control vs VLBW group (95% CI)	Model 3 *P*-values
Sleep end	min:s	−40:13 (−70:47 to −09:39)	0.011	−39:54 (−71:40 to −08:08)	0.015	−38:40 (−72:30 to −04:51)	0.026
Get up time	min:s	−40:01 (−71:04 to −08:58)	0.012	−39:47 (−72:03 to −7:31)	0.016	−39:05 (−73:17 to −04:53)	0.026
Sleep start	min:s	−18:51 (−52:31 to 14:48)	0.27	−23:43 (−58:13 to 10:46)	0.18	−26:19 (−62:16 to 9:39)	0.15
Bed time	min:s	−00:10 (−29:59 to 29:38)	0.99	−01:42 (−32:01 to 28:37)	0.91	−05:18 (−36:52 to 26:17)	0.74
Actual sleep time	min:s	−14:30 (−38:50 to 09:50)	0.24	−8:36 (−32:51 to 15:39)	0.48	−7:09 (−33:54 to 19:36)	0.60
Sleep latency	(%)[a]	−15.8 (−54.3 to 55.2)	0.58	−19.6 (−57.1 to 50.9)	0.49	−0.77 (−50.82 to 100.3)	0.98
Sleep efficiency	%	0.97 (−2.2 to 4.2)	0.55	1.4 (−1.9 to 4.6)	0.41	0.37 (−2.9 to 3.6)	0.82
WASO	min:s	−05:43 (−18:07 to 06:41)	0.36	−06:18 (−19:10 to −6:34)	0.33	−04:22 (−18:15 to 9:31)	0.53
Fragmentation index		−0.63 (−5.3 to 4.0)	0.79	−0.81 (−5.7 to 4.0)	0.74	−1.0 (−6.0 to 4.0)	0.69

VLBW, very low birthweight; CI, confidence interval; WASO, wake after sleep onset.
A negative value indicates an earlier time or shorter duration in the VLBW group.
Model 1: unadjusted.
Model 2: adjusted for sex and age.
Model 3: full model (sex, age, parental education, current smoking, use of antidepressants and state of employment), missing $n = 5$, 3 men, 2 women.
[a] Because sleep latency had a right-skewed distribution, it was log-transformed, and geometric mean with mean difference in percent is reported.

roborated the findings of morningness propensity among 13-year-olds born preterm [35].

The mechanisms underlying our findings remain speculative. The premature child is subjected to a host of influences after birth, and is at the same time deprived of essential maternal influences that would have existed in utero for weeks or months before a term birth would have taken place. These conditions may affect the maturating mechanisms underlying sleep development. One possible mechanism is the wide prevalence of constant lighting that was used in the NICUs of the era in which our subjects were born. Animal models have shown the influences of postnatal light on the developing suprachiasmatic nucleus, the organ considered the body's primary timekeeper [36–38]. Prematurely born infants are also deprived of maternal melatonin, which is an important circadian regulator and tissue protector. Whereas all children to a degree have low melatonin levels during the first 2–4 months of life, the effect of an even more prolonged deficiency due to premature parturition might be of interest [39].

We cannot exclude the possibility that chronotype, being partially genetically mediated [40], and prematurity share a common genetic origin. Another possible interpretation of the data is that infants with early chronotype for some reason may be more likely to survive a preterm birth.

Potentially, our findings of earlier wake-up times among the ex-preterms, in combination with the lack of significant difference in bedtimes, may partly be attributable to shorter sleep duration among the ex-preterms. However, it is unclear whether our finding reflects shorter sleep duration, since it did not differ significantly between the groups, and since previous studies using questionnaire have produced results similar to ours [22,35].

Strengths of this study include the well-described cohort of VLBW subjects and term-born controls, with extensive background data available. Furthermore, by using actigraphy, we achieved objective information on sleep patterns.

Limitations include possible participation bias since the study was performed on a subsample of the original cohort. However, the subsample in the current study did not differ from the rest of the study participants of the follow-up study with regard to most background variables, the only perceived difference being that the participants in the actigraphy study reported more frequently as being in paid employment than the non-participants. Another issue under debate is whether three measured nights are enough for a reliable analysis of sleep characteristics [41]. Whereas some have concluded that at least 3 nights are needed [31], others recommend more than 7 days of registration for an acceptable reliability of interday stability [42]. Further limitations include the relatively small sample size, and the inability to control for potential confounders that may affect sleep–wake cycles, such as work start time, commuting time, time needed to get ready in the morning, etc. Our results need to be confirmed using experimental settings using objective markers of circadian phase. Nonetheless, epidemiologic studies are needed to identify the phenomenon and to generate hypotheses to be tested in future clinical studies.

In conclusion, very low birth weight seems to be associated with an advanced sleep phase in young adulthood. Although the underlying mechanisms are unknown, an advanced sleep phase might have far-reaching effects on the health of the prematurely born in general, as morningness is associated with beneficial health outcomes [43,44]. The finding contributes to understanding the development of sleep and circadian rhythms.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.04.016.

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